B6

14. A method of treating a disease mediated by farnesylation of mutant ras gene comprising administering an effective amount of a compound of Formula I according to claim 1.

15. A method of treating a disease mediated by farnesylation of mutant ras gene comprising administering an effective amount of a compound according to claim 3.

16. A method of treating a disease mediated by farnesylation of mutant ras gene comprising administering an effective amount of a compound of formula A according to claim 7.

17. A method of treating a disease mediated by farnesylation of mutant ras gene comprising administering an effective amount of a compound according to claim 8.

REMARKS

I. Status of the Claims

Claims 1, 3 and 7-17 are pending in the present application.

Claims 2, 4, 5, and 6 have been canceled without disclaimer or prejudice to claim the subject matter in a continuing application.

Claims 1, 3, 7, 8, 9, 11, and 12 have been amended and no new matter has been added.

Claims 14, 15, 16, and 17 have been added and no new matter has been introduced.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

II. Rejection of Impr per Markush Grouping

The Examiner has objected to claims 1, 3, and 7-13 as containing an improper Markush grouping. Applicants deletion of non-elected subject matter has overcome this rejection; therefore, withdrawal of this rejection is respectfully requested.

III. Rejection Under 35 U.S.C. § 112 First Paragraph

A. The Examiner has rejected claims 1, 3, and 9-13 under 35 U.S.C. §112, first paragraph. Specifically, the Examiner asserts that the scope of "prodrug" is not adequately enabled. In addition, the Examiner suggests that Applicants have failed to provide guidance to make the compounds active *in vivo*. Applicants respectfully traverse this rejection.

Various forms of prodrugs are well known in the art and Applicants have incorporated by reference examples of such prodrugs (Applicants direct the Examiner to page 23, lines 3 to 22 of the present application). Contrary to the position taken by the Examiner, it is not necessary for Applicants to provide a specific example of everything within the scope of the claim. In re Anderson, 471 F.2d 1237, 176 U.S.P.Q 331, (CCPA 1973). The proper inquiry is whether the experimentation needed to practice the invention is undue or unreasonable. In re Wands, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Applicants assert that little or no experimentation would be necessary to practice the present invention as claimed. When rejecting a claim under the enablement requirement of §112, the Examiner bears "the initial burden of setting forth a reasonable explanation as to why [he/she] believes that the scope of the protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification." In re Wright, 999 F.2d 1557, 1562, 27

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). To object to a specification on the grounds that the disclosure is not enabling with respect to the scope of the claim sought to be patented, the Examiner must provide evidence or technical reasoning substantiating those doubts. MPEP §2164.04. Therefore, without a reason to doubt the truth of the statements made in the patent application, the present application must be considered enabling. In re Wright, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). Therefore, Applicants respectfully request withdrawal of this rejection.

B. The Examiner has further rejected claims 9 and 12 under 35 U.S.C. §112, first paragraph, for lack of enablement in treating disorders associated with farnesylation of mutant ras. The Examiner asserts that the art does not recognize use of such inhibitors as broad based drugs for treating all disorders instantly embraced. Applicants respectfully traverse this rejection.

Applicants direct the attention of the Examiner to cited U.S. Patent No. 5,929,077 column 5 lines 45 to column 6 line 6. The '077 patent teaches use of thioproline compounds as a model to treat various disorders associated with farnesylation of the ras gene, including bladder, breast, colon, rectum, kidney, liver, lung, ovary, pancreas, stomach, cervix, thyroid and skin cancers. Therefore, contrary to the position taken by the Examiner, the art does recognize use of such inhibitors as broad based drugs for treating all disorders embraced in the present invention.

Further, Applicants direct the Examiner's attention to the decision of the Court of Customs and Patent Appeals in In re Marzocchi, 439 F.2d 20, 169 U.S.P.Q. 367 (CCPA 1971). The Court held:

> In the field of chemistry, generally there may be times when the well known unpredictability of chemical reactions will

LAW OFFICES
FINNEGAN, HENDERSON, FARABOW, GARRETT, & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

> alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof. In any event, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure....

Marzocchi, 439 F.2d at 22, 367 U.S.P.Q. at 369-70 (emphasis added) (citations omitted).

Applicants ask that the Examiner point to any available references showing that one of ordinary skill in the art would doubt the accuracy of Applicants asserted discovery of activity of the presently claimed compounds as farnesyl protein transferase inhibitors. Applicants respectfully request withdrawal of this rejection.

IV. Rejection Under 35 U.S.C. § 112 Second Paragraph

Amendment of claims 1, 3, 7, 8, 9, 11, and 12 should overcome Examiner's rejection.

The Examiner has also rejected claims 11 and 12 as being vague, specifically usage of the term "medicament". Applicants respectfully traverse this rejection.

Applicants direct the Examiner's attention to page 27, lines 28-30 wherein "medicament" is described within the scope of the present invention. Applicants

LAW OFFICES
FINNEGAN, HENDERSON, FARABOW, GARRETT, & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

suggest that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. In re Marosi, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983); Rosemount, Inc. v. Beckman Instruments, Inc., 727 F.2d 1540, 221 U.S.P.Q.1 (Fed. Cir. 1984); W.L. Gore & Asocs., Inc v. Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983).

V. Rejection Under 35 U.S.C. § 103

The Examiner has rejected claims 1, 3 and 7-13 under 35 U.S.C. §103(a) as being unpatentable over Leftheris, U.S. Patent No. 5,929,077. The Examiner asserts that it would be obvious to one of ordinary skill in the art to modify the mercapto moiety substituted in the 4-position of the pyrrolidine ring in the teachings of Leftheris with the 3-position in the pyrrolidine ring to derive the presently claimed invention. This rejection is respectfully traversed.

The Examiner has failed to specifically point out the basis of motivation for one of ordinary skill in the art to modify the prior art to derive the claimed invention. "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination". In re Geiger, 815 F.2d 686, 688, 2 U.S.P.Q.2d 1276, 1278 (Fed.Cir.1987); In re Laskowski, 871 F.2d 115, 117, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989) ("[t]he mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification) (quoting In re Gordon, 733 F2.d 900, 902, 221 U.S.P.Q. 1125, 1127

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

(Fed.Cir.1984)); Sentex Systems, Inc. v. Elite Access Systems, Inc., 1999 U.S. App. LEXIS 3846 at *17.

The Examiner may rely on logic and sound scientific principles in support of a rejection under §103. See In re Soli, 317 F.2d 941, 947, 137 U.S.P.Q 797, 801 (C.C.P.A. 1963). But the Examiner must provide some evidentiary basis for the existence and meaning of the scientific principle relied on. See In re Grose, 592 F.2d 1161, 1167-68, 201 U.S.P.Q. 57, 63 (C.C.P.A. 1979). "That one can reconstruct and/or explain the theoretical mechanism of an invention by means of logic and sound scientific reasoning does not afford the basis for an obviousness conclusion unless that logic and reasoning also supplies sufficient impetus to have led one of ordinary skill in the art to combine the teachings of the references to make the claimed invention." Ex parte Levengood, 28 U.S.P.Q.2d 1300, 1302 (Bd. Pat. App. & Int. 1993). The Examiner merely suggests that the 4- and the 3-position of the mercapto moiety **would be expected** to share common properties absent showing unexpected results. The Examiner has not provided any sound scientific reasoning nor does the Examiner show that the teachings of the prior art supply sufficient impetus to have led one of ordinary skill in the art to make the claimed invention.

Further, as a general matter, isomerism by itself should not raise a *prima facie* case of obviousness. Ex parte Mowry, 91 U.S.P.Q. 219, 221 (Bd. Pat. App. 1950) (rejecting the proposition that isomers in the broad sense are necessarily equivalent and holding claimed cyclohexylstyrene unobvious over prior art isohexylstyrene). Indeed, the Federal Circuit has admonished against generalizing, especially in the area of chemical structural obviousness, requiring proof in the prior art to support a proposed

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

structural change. See In re Grabiak, 769 F.2d 729, 731-32, 226 U.S.P.Q. 870, 872 (Fed. Cir. 1985).

Applicants point out that the Leftheris patent teaches away from the present claimed invention. The '077 patent teaches a mercapto moiety substituted on the **4**-position of the **pyrrolidine** ring in examples 1, 4, 5, 6, 7, and 8. However when examining examples 2 and 3, Leftheris specifically substituted a mercapto moiety in the 3-position of a non-pyrrolidine system, but instead teaches a substitution of mercapto moiety in a cyclopentyl system. Therefore, had the 3-position of the mercapto moiety on a pyrrolidine ring been obvious, the '077 patent would not change the ring system. Withdrawal of this rejection is respectfully requested.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: September 4, 2001

By: Charles E Van Horn

Charles E. Van Horn
Reg. No. 40, 266

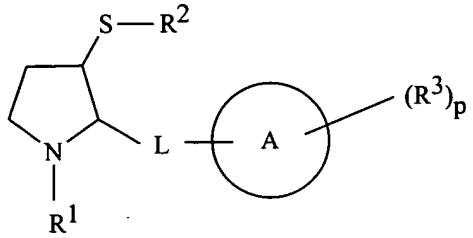
LAW OFFICES
FINNEGAN, HENDERSON, FARABOW, GARRETT, & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Appendix I: Claims

(materials within brackets are deleted and materials that are underlined are added)

Claim 1:

1. A compound of the Formula I



Formula I

wherein:

R^1 is selected from H; -C_{1-4}alkyl; -CO-C_{1-4}alkyl; -CO-O-C_{1-4}alkyl; -CO-O-C_{2-4}alkenyl; -C_{1-4}alkylene-$CONR^4R^5$ (wherein R^4 and R^5 are independently selected from H and C_{1-4}alkyl); -C_{1-4}alkylene-$COOR^6$ (wherein R^6 is selected from H and C_{1-4}alkyl); -C_{1-3}alkylene-Ph and -CO-O$(CH_2)_n$Ph wherein the phenyl groups in -C_{1-3}alkylene-Ph and -CO-O$(CH_2)_n$Ph are optionally substituted by R^a and/or R^b and R^a and R^b are independently selected from C_{1-4}alkyl, halogen, hydroxy, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, C_{1-4}alkanoylamino, nitro, cyano, carboxy, carbamoyl, C_{1-4}alkoxycarbonyl, thiol, C_{1-4}alkylsulfanyl, C_{1-4}alkylsulfinyl,C_{1-4}alkylsulfonyl and sulfonamido; and n=0-4;

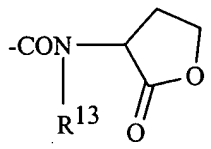
R^2 is selected from H; -C_{1-4}alkyl; -COC_{1-4}alkyl; and -$COOC_{1-4}$alkyl; and -C_{1-3}alkylene-Ph optionally substituted on the phenyl ring by R^a and/or R^b;

R^3 is selected from H; OH; CN; CF_3; NO_2; -C_{1-4} alkyl; -C_{1-4}alkylene-R^7; -C_{2-4}alkenylene-R^7; -C_{2-4}alkynylene-R^7; R^7; OR^7 (where R^7 is selected from phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing upto 5 heteroatoms selected from O,N and S and any aryl ring in R^7 is optionally substituted by R^a and/or R^b); C_{2-4}alkenyl; halogen; -$(CH_2)_n COOR^8$ (where [n^1] n = 0-3 and R^8

LAW OFFICES
FINNEGAN, HENDERSON, FARABOW, GARRETT, & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

represents H, C_{1-4}alkyl, or C_{2-4}alkenyl); -$CONR^9R^{10}$ (where R^9 and R^{10} independently represent H, C_{1-4}alkyl, C_{2-4}alkenyl, -O-C_{1-4}alkyl, -O-C_{2-4}alkenyl or -C_{1-3}alkylenePh (wherein Ph is optionally substituted by R^a and R^b as hereinabove defined);-$CON(R^{11})OR^{12}$ (where R^{11} and R^{12} independently represent H, C_{1-4}alkyl or C_{2-4}alkenyl);

[a group of Formula II:] -$CONR^{13}$-$CR^{13a}R^{14}$-$COOR^{17}$, (where R^{13} and R^{13a} are independently H or C_{1-4}alkyl, R^{17} is H or C_{1-6}alkyl, R^{14} is selected from the side chain of a lipophilic amino acid, carbamoylC_{1-4}alkyl, N-(monoC_{1-4}alkyl)carbamoylC_{1-4}alkyl and N-(diC_{1-4}alkyl)carbamoylC_{1-4}alkyl) [the group of Formula II] having L or D configuration at the chiral alpha carbon in the corresponding free amino acid; a lactone of formula:



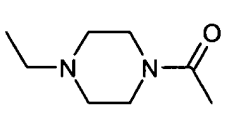
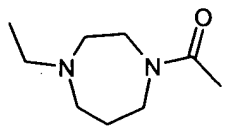
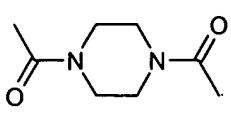
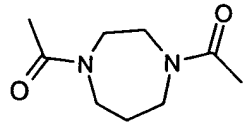
;

C_{1-4}alkyl monosubstituted on carbon with =N-OH;

a group of Formula -X-R^{15} (where X is selected from O, CO, CH_2, S, SO, SO_2 and R^{15} is selected from C_{1-6}alkyl, phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing upto 5 heteroatoms selected from O,N and S and any aryl ring in R^{15} is optionally substituted by R^a and/or R^b;

p is 0-3 in which R^3 values can be the same or different;

L is a linking moiety selected from the following groups written from left to right in Formula I:


;

;

;

;

(wherein the piperazine and perhydro-1,4-diazepine rings are optionally substituted);

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

-CO-NR^{16}-; -CH_2-NR^{16}- ; -CH_2S-; -CH_2O-; -CH_2-CHR^{16}; -CH=CR^{16}-; -CH_2NR^{16}-T-; -CH_2NR^{16}-SO_2-; -CH_2-NR^{16}-CO-T^1-; -CO-NR^{16}-T-; -CH_2S-T-; -CH_2O-T- (where R^{16} is selected from H, C_{1-4}alkyl, C_{1-4}alkylene-Z, -CO-C_{1-4}alkylene-Z, -CO-C_{1-6}alkyl, -COZ, Z and Z is selected from -O-C_{1-4}alkyl, phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing upto 5 heteroatoms selected from O, N and S and any aryl ring in R^{16} is optionally substituted by R^a and/or R^b as hereinabove defined; where, T represents -(CH_2)m- where m is 1-4 and T is optionally monosubstituted with any value of R^{16} other than H; and
where T^1 represents -(CH_2)m^1- wherein m^1 is 0-4 and T is optionally monosubstituted with any value of R^{16} other than H);
A is selected from phenyl; naphthyl; a 5-10 membered monocyclic or bicyclic heteroaryl ring containing upto 5 heteroatoms where the heteroatoms are independently selected from O, N & S;
or a -S-S- dimer thereof when R^2=H; or a N-oxide thereof;
or a pharmaceutically acceptable salt, prodrug or solvate thereof.

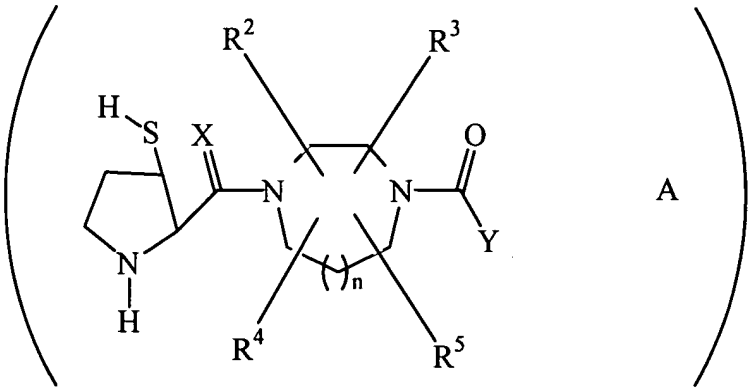
Claim 3:

3. A compound according to [either] claim 1 [or claim 2] wherein A is phenyl or naphthyl.

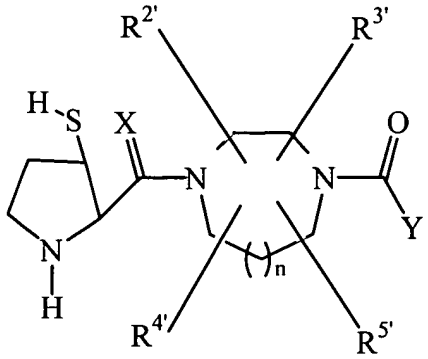
Claim 7:

7. A compound of the formula A:

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000



A



A

---

wherein:

X is O or H_2;

n is 0 or 1;

t is 1 to 4;

$R^{2'}$, $R^{3'}$, $R^{4'}$, and $R^{5'}$ are independently selected from: H; C_{1-8}alkyl, alkenyl, alkynyl, aryl, heterocycle, -CO-$NR^{6'}R^{7'}$ or -CO-$OR^{6'}$, unsubstituted or substituted with one or more of:

1) aryl or heterocycle, unsubstituted or substituted with:
   a. C_{1-4}alkyl,
   b. $(CH_2)_tOR^{6'}$,
   c. $(CH_2)_tNR^{6'}R^{7'}$,
   d. halogen,

LAW OFFICES
FINNEGAN, HENDERSON, FARABOW, GARRETT, & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

2) C_{3-6}cycloalkyl,

3) $OR^{6'}$,

4) $SR^{6'}$, $S(O)R^{6'}$, $SO_2R^{6'}$,

5) $-NR^{6'}R^{7'}$,

6) $-NR^{6'}-CO-R^{7'}$,

7) $-NR^{6'}-CO-NR^{7'}R^{8'}$,

8) $-O-CO-NR^{6'}R^{7'}$,

9) $-O-CO-OR^{6'}$,

10) $-O-NR^{6'}R^{7'}$,

11) $-SO_2NR^{6'}R^{7'}$,

12) $-NR^{6'}-SO_2-R^{7'}$,

13) $-CO-R^{6'}$, or

14) $-CO-OR^{6'}$;

and any two of $R^{2'}$, $R^{3'}$, $R^{4'}$, and $R^{5'}$ are optionally attached to the same carbon atom;

Y is aryl, heterocycle, unsubstituted or substituted with one or more of:

1) C_{1-4}alkyl, unsubstituted or substituted with:

   a. C_{1-4}alkoxy,

   b. $NR^{6'}R^{7'}$,

   c. C_{3-6}cycloalkyl,

   d. aryl or heterocycle,

   e. HO,

2) aryl or heterocycle,

3) halogen,

4) $OR^{6'}$,

5) $NR^{6'}R^{7'}$,

6) CN

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

7) NO_2, or

8) CF_3;

$R^{6'}$, $R^{7'}$ and $R^{8'}$ are independently selected from: H; C_{1-4}alkyl, C_{3-6}cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

a) C_{1-4}alkoxy,

b) aryl or heterocycle,

c) halogen,

d) HO,

e) $-CO-R^{9'}$,

f) $-SO_2R^{9'}$, or

[g) NRR^1,] wherein

$R^{6'}$ and $R^{7'}$ may be joined in a ring, and

$R^{7'}$ and $R^{8'}$ may be joined in a ring;

$R^{9'}$ is C_{1-4}alkyl or aralkyl;

a pharmaceutically acceptable salt thereof.

Claim 8:

8. A compound according to claim 1 which is any one of the following individual compounds or a pharmaceutically acceptable salt thereof:

(2S)-2-{2-benzyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester ;

(2S)-2-{2-benzyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid ;

(2S)-2-({2-phenyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid methyl ester;

LAW OFFICES
FINNEGAN, HENDERSON, FARABOW, GARRETT, & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

(2S)-2-({2-phenyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid;

(2S)-2-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl)amino]-naphthalene-1-carbonyl}-amino)-4-methylsulfanylbutyric acid methyl ester ;

(2S)-2-({3-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl)amino]-naphthalene-1-carbonyl}-amino)-4-methylsulfanylbutyric acid ;

(2S)-2-({-3-phenyl-5[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid methyl ester;

(2S)-2-({-3-phenyl-5[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid;

(cis)-2-[{N-(4-methoxybenzyl)- N-(naphthalen-1-ylmethylamino}-methyl]-pyrrolidine-3-thiol ;

N-(naphthalen-1-ylmethyl)-N-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl)-pentanamide;

N-(naphthalen-1-ylmethyl)-N-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl)-2-(pyridin-3-yl)-acetamide ;

N-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-3-methyl-N-(2-naphthalen-1-yl-ethyl)butyramide ;

N-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-N-(2-naphthalen-1-yl-ethyl)-2-pyridin-3-yl-acetamide ;

(cis)-2-{[(3-methoxypropyl)-(2-naphthalen-1-ylethyl)amino]methyl}- pyrrolidine-3-thiol;

N-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-2-(4-methoxy-phenyl)-N-(2-naphthalen-2-yl-ethyl)-acetamide;

(cis)-2-{[(2-(4-methoxyphenyl)ethyl)-(2-naphthalen-1-ylethyl)amino] methyl}- pyrrolidine-3-thiol;

N-(2,2-diphenyl-ethyl)-N-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-3-methyl-butyramide ;

N-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-3,3-dimethyl-N-(2-naphthalen-2-yl-ethyl)-butyramide;

N-(2,2-diphenyl-ethyl)-N-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-3,3-dimethyl-butyramide;

(2S)-2-{3-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-(3-methoxy-propyl)-amino]-benzoylamino}-4-methylsulfanyl-butyric acid ;

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

N-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-3,3-dimethyl-N-(2-naphthalen-1-yl-ethyl)-butyramide;

(2S)-4-carbamoyl-2-({2-phenyl-5-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-butyric acid;

(2S)-4-carbamoyl-2-({2-phenyl-5-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-butyric acid methyl ester;

2-(3-pyridyl)-N-(2,2-diphenyl-ethyl)-N-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl)- acetamide;

6-methoxy-1-oxido-N-(2,2-diphenyl-ethyl)-N-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl]-pyridine-3-carboxamide;

N-(naphthyl-1-yl-ethyl)-N-[(cis)-3-sulfanylpyrrolidin-2yl-methyl)-thiazole-5-carboxamide;

6-methoxy-1-oxido-N-(naphthyl-1-yl-ethyl)-N-[cis)-3-sulfanylpyrrolidin-2-ylmethyl]-pyridine-3-carboxamide;

(2S)-2-{2-benzyl-4-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl[)]amino]-benzoylamino}-4-methylsulfanyl-butyric acid;

[(2S)-2-(2-methoxy-ethyl)-1-[(cis)-3-sulfanyl-pyrrolidin-2-ylmethyl[)]]-4-naphthoyl-piperazine;]

(2S)-2-{2-benzyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl)amino]-benzoylamino}-4-methylsulfanylbutyric acid;

(2S)-2-{2-benzyl-4-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl)amino]-benzoylamino}-4-methylsulfanylbutyric acid;

(2S)-2-{2-phenethyl-5-[(trans)-3-sulfanylpyrrolidin-2-ylmethylaminobenzoylamino}-4-methylsulfanylbutyric acid;

(2S)-2-{phenethyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid;

(2S)-2-{2-benzyl-5-[(trans)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid;

(2S)-2-{2-(phenethyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid;

(2S)-2-{2-(4-methylphenylethynyl)-4-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid;

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

(2S)-2-{2-benzyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid isopropyl ester;
(2S)-2-{2-benzyl-4-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-{2-benzyl-4-[(trans)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-{2-benzyl-5-[(trans)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-{2-phenyl-5-[(trans)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-{2-phenyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-{2-benzyl-5-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-{2-(4-methylphenethyl)-4-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-{2-(4-methylphenylethynyl)-4-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl[()]amino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester;
(2S)-2-(2-methoxyethyl)-1-[(cis)-3-sulfanylpyrrolidin-2-ylmethyl[()]]-4-(naphth-1-oyl)piperazine;
(cis)-2-[N-isovaleryl-N-(2-(napth-1-yl)ethyl)aminiomethyl]-3-sulfanylpyrrolidine;
(cis)-2-[N-(3-pyridylacetyl)-N-(naphth-1-yl)ethyl)aminomethyl]-3-sulfanylpyrrolidine;
(cis)-2-[N-1-oxido-6-methoxypyridin-3-ylcarbonyl) -N-(naphth-1-yl)ethyl)aminomethyl]-3-sulfanylpyrrolidine;
(cis)-2-[N-thiazol-5-ylcarbonyl) -N-(naphth-1-yl)ethyl)aminomethyl]-3-sulfanylpyrrolidine;
(2S)-2-[2-(4-fluorophenethyl)-4-[(cis)-3-sulfanyl)-pyrrolidin-2-ylmethylamino)benzoylamino]-4-methylsulfanylbutyric acid;
methyl (2S)-2-[2-(4-fluorophenethyl)-4-[(cis)-3-sulfanylpyrrolidin-2-ylmethylamino)benzoylamino]-4-methylsulfanylbutyrate;
(2S)-2-[2-(4-fluorophenethyl)-4-((2R,3R)-3-sulfanyl-pyrrolidin-2-ylmethylamino)benzoylamino]-5-methylsulfanylbutyric acid;

LAW OFFICES
FINNEGAN, HENDERSON, FARABOW, GARRETT, & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

(2S)-2-{2-Benzyl-5-[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-benzoylamino}-4-methylsulfanylbutyric acid methyl ester ;

(2S)-2-{2-Benzyl-5-[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-benzoylamino}-4-methylsulfanylbutyric acid ;

(2S)-2-({2-phenyl-5-[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid methyl ester;

(2S)-2-({2-phenyl-5-[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid;

(2S)-2-({3-[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-naphthalene-1-carbonyl}-amino)-4-methylsulfanylbutyric acid methyl ester ;

(2S)-2-({3-[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-naphthalene-1-carbonyl}-amino)-4-methylsulfanylbutyric acid ;

(2S)-2-({-3-phenyl-5[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid methyl ester;

(2S)-2-({-3-phenyl-5[([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-4-methylsulfanylbutyric acid;

(2R,3R)-2-[{N-(4-methoxybenzyl)- N-(naphthalen-1-ylmethyl)-amino}-methyl]-pyrrolidine-3-thiol ;

N-(naphthalen-1-ylmethyl)-N-([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-pentanamide;

N-(naphthalen-1-ylmethyl)-N-([2R,3R]-3-sulfanylpyrrolidin-2-ylmethyl)-2-(pyridin-3-yl)-acetamide ;

N-((2R,3R)-3-sulfanyl-pyrrolidin-2-ylmethyl)-3-methyl-N-(2-naphthalen-1-yl-ethyl)butyramide ;

N-([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-N-(2-naphthalen-1-yl-ethyl)-2-pyridin-3-yl-acetamide ;

(2R,3R)-2-{[(3-Methoxypropyl)-(2-naphthalen-1-ylethyl)amino]methyl}- pyrrolidine-3-thiol;

N-([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-2-(4-methoxy-phenyl)-N-(2-naphthalen-2-yl-ethyl)-acetamide ;

(2R,3R)-2-{[(2-(4-Methoxyphenyl)ethyl)-(2-naphthalen-1-ylethyl)amino] methyl}-pyrrolidine-3-thiol ;

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

N-(2,2-Diphenyl-ethyl)-N-([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-3-methyl-butyramide ;

N-([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-3,3-dimethyl-N-(2-naphthalen-2-yl-ethyl)-butyramide ;

N-(2,2-Diphenyl-ethyl)-N-([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-3,3-dimethyl-butyramide ;

(2S)-2-{3-[([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-(3-methoxy-propyl)-amino]-benzoylamino}-4-methylsulfanyl-butyric acid ;

N-([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-3,3-dimethyl-N-(2-naphthalen-1-yl-ethyl)-butyramide ;

(2S)-4-carbamoyl-2-({2-phenyl-5-[([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-butyric acid;

(2S)-4-carbamoyl-2-({2-phenyl-5-[([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-amino]-phenylcarbonyl}-amino)-butyric acid methyl ester;

2-(3-pyridyl)-N-(2,2-diphenyl-ethyl)-N-((2R,3R)-3-sulfanylpyrrolidin-2-ylmethyl)-acetamide;

6-methoxy-1-oxido-N-(2,2-diphenyl-ethyl)-N-((2R,3R)-3-sulfanylpyrrolidin-2-ylmethyl)-pyridine-3-carboxamide;

N-(naphthyl-1-yl-ethyl)-N-([2R,3R]-3-sulfanylpyrrolidin-2yl-methyl)-thiazole-5-carboxamide;

6-methoxy-1-oxido-N-(naphthyl-1-yl-ethyl)-N-((2R,3R)-3-sulfanylpyrrolidin-2-ylmethyl)-pyridine-3-carboxamide;

(2S)-2-{2-benzyl-4-[([2R,3R]3-sulfanyl-pyrrolidin-2-ylmethyl)-amino]-benzoylamino}-4-methylsulfanyl-butyric acid; and

(2S)-2-(2-methoxy-ethyl)-1-([2R,3R]-3-sulfanyl-pyrrolidin-2-ylmethyl)-4-naphthoyl-piperazine.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Claim 9:

10. A pharmaceutical composition which comprises a compound according to any one of claims [1 to 8] 1, 3, 7, or 8 and a pharmaceutically-acceptable carrier.

Claim 11:

11. A compound according to any one of claims [1 to 8] 1, 3, 7 or 8 for use as a medicament.

Claim 12:

12. A compound according to any one of claims [1 to 8] 1, 3, 7 or 8 for use in the preparation of a medicament for treatment of a disease mediated through farnesylation of mutant ras.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000